

<110> Pecker, Iris

2

Vlodavsky , Israel

Feinstein, Elena

<120> POLYNUCLEOTIDE ENCODING A POLYPEPTIDE HAVING HEPARANASE ACTIVITY AND EXPRESSION OF SAME IN GENETICALLY MODIFIED CELLS

<130> 27674

<160> 49

<170> PatentIn version 3.1

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<213> Homo sapiens

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<213> Homo sapiens

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Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro $20 \hspace{1cm} 25 \hspace{1cm} 30 \hspace{1cm}$

Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro $35 \hspace{1cm} 40 \hspace{1cm} 45 \hspace{1cm}$

Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn 50

Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu 65 70 70 75

Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe $100 \\ 0.05$

Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys Phe 145 \$150\$

Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe \$165\$

Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu 180 \$180\$

Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu 195 200

Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn 210 $\,$ 220 $\,$

Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser 225 230235235

Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Glu 275 \$280\$ 285

4

Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr $290 \hspace{1.5cm} 295 \hspace{1.5cm} 300 \hspace{1.5cm}$

Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile 305 \$310\$

Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly $325 \hspace{1.5cm} 330 \hspace{1.5cm} 335$

Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala $340 \hspace{1cm} 345 \hspace{1cm} 345 \hspace{1cm} 350 \hspace{1cm}$

Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys 355 $$ 365

Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val 370 \$375\$

Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr $405 \ \ \, 410 \ \ \, 415$

Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg 420 425 430

Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly $435 \ \ \, 440 \ \ \, 445$

Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu 465 470470

Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn $485 \hspace{1.5cm} 490 \hspace{1.5cm} 495$

Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met $500 \hspace{1.5cm} 505 \hspace{1.5cm} 510 \hspace{1.5cm}$

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tcg cag tta gga gaa gat tat att caa ttg cat aaa ctt cta aga aag Ser Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys 240 245 250 255	827
tcc acc ttc aaa aat gca aaa ctc tat ggt cct gat gtt ggt cag cct Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro 260 265 270	875
cga aga aag acg gct aag atg ctg aag agc ttc ctg aag gct ggt gga Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly 275 280 285	923
gaa gtg att gat tca gtt aca tgg cat cac tac tat ttg aat gga cgg Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg 290 295 300	971
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gcg ccc ttg cta tcc gac acc ttt gca gct ggc ttt atg tgg ctg gat Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp 355 360 365	1163
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cct tta cct gat tat tgg cta tct ctt ctg ttc aag aaa ttg gtg ggc Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly 400 405 410 415	1307
acc aag gtg tta atg gca agc gtg caa ggt tca aag aga agg aag ctt Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu 420 425 430	1355
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gga gat tta act ctg tat gcc ata aac ctc cat aac gtc acc aag tac Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr 450 455 460	1451
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824

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<212> PRT

<213> Homo sapiens

<400> 14

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Arg Arg Lys Gly Arg Trp Gly Ser Ala Gly Gly Ser Ala Arg Ala Leu $20 \hspace{1cm} 25 \hspace{1cm} 30$

Asp Ser Pro Leu Arg Gly Ser Trp Arg Gly Glu Gln Pro Gly Glu Pro 35 40 45

Lys Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu 50 60

Leu Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg 65 70707575

Pro Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu 85 90 95

Pro Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala 100 105 105

Asn Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Gly Ser Pro Lys 115 120 125

Leu Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly 130 135

Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr 145 150150155

Phe Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys 165 170 175

Lys Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu 180 185 190

Trp Pro Tyr Gln Glu Gln Leu Leu Leu Arg Glu His Tyr Gln Lys Lys 195 200 205

Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr 210 215 220

Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu 225 230235235

Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu 245 255

Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly 260 265 270

Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly 275 280 285

Ser Gln Leu Gly Glu Asp Tyr Ile Gln Leu His Lys Leu Leu Arg Lys 290 295 300

Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro 305 310310315

Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly $325 \hspace{1cm} 330 \hspace{1cm} 335 \hspace{1cm}$

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Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly 385 390395

Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp 405 410 415

Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp 435 440445

Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly 450 450

Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu

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							cca Pro									498
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							gcg Ala									834
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Ala Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp $20 \\ 25 \\ 30$

Leu Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe $35 \ \ \, 40 \ \ \, 45$

Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu 50 55

Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser 65 70 75 80

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe $85 \\ 0 \\ 0 \\ 95$

Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser 100 $$105\ \ \, 100$$

Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val 115 120 125

Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu 130 135 140

Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser 145 \$150\$ 155 160

Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu 165 \$170\$

Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn 180 $$185\$

Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr 195 200

Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys 210 215 220

Ala His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu 225 230235235

Leu His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr $245 \hspace{1.5cm} 250 \hspace{1.5cm} 255 \hspace{1.5cm}$

Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg $260 \hspace{1cm} 265 \hspace{1cm} 265 \hspace{1cm} 270 \hspace{1cm}$

Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His 275 280 285

His Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser 290 295 300

Ser Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys 305 310 310

Val Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr \$325\$ \$330 \$335

Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala $340 \hspace{1.5cm} 345 \hspace{1.5cm} 350$

Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly 355 360 365

Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His $370 \ \ 380$

Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu 385 $$ 390 $$ 395 $$ 400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys $405 \hspace{0.25cm} 410 \hspace{0.25cm} 410 \hspace{0.25cm} 415 \hspace{0.25cm}$

Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val $420 \hspace{1.5cm} 425 \hspace{1.5cm} 430$

Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn 435

Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg 450 $\,$ 460 $\,$

Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu 465 $$ 470 $$ 475 $$ 480

Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp 485 490 495

Ala Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn 515 520 525

Ala Lys Ile Ala Ala Cys Ile 530 535

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Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe Leu
35 40 tcc atc acc atc gac gcc agc ctg gcc acc gac ccg cgc ttc ctc acc Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu Thr 50 55 60 65ttc ctg ggc tct cca agg ctc cgt gct ctg gct aga ggc tta tct cct Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser Pro 70 75 80gca tac ttg aga ttt ggc ggc aca aag act gac ttc ctt att ttt gat Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp 85 90 90 95ccg gac aag gaa ccg act tcc gaa gaa agt tac tgg aaa tct caa Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser Gln 100 105 110gtc aac cat gat att tgc agg tct gag ccg gtc tct gcg gcg gtg ttg Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val Leu 115 120 125agg aaa ctc cag gtg gaa tgg ccc ttc cag gag ctg ttg ctg ctc cga Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu Arg 130 135 1451028 gag cag tac caa aag gag ttc aag aac agc acc tac tca aga agc tca Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser 150 150 160gtg gac atg ctc tac agt ttt gcc aag tgc tcg ggg tta gac ctg atc Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu Ile 165 170 175ttt ggt cta aat gcg tta cta cga acc cca gac tta cgg tgg aac agc Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn Ser 180 180 185 190tcc aac gcc cag ctt ctc ctt gac tac tgc tct tcc aag ggt tat aac Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn 195 200 205

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					ggg Gly											1316
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					gga Gly											1460
					cgc Arg 295											1508
					ttt Phe											1556
act Thr	aaa Lys	gag Glu	atc Ile 325	aca Thr	cct Pro	ggc Gly	aag Lys	aag Lys 330	gtc Val	tgg Trp	ttg Leu	gga Gly	gag Glu 335	acg Thr	agc Ser	1604
					ggt Gly											1652
ggc Gly	ttt Phe 355	atg Met	tgg Trp	ctg Leu	gat Asp	aaa Lys 360	ttg Leu	ggc Gly	ctg Leu	tca Ser	gec Ala 365	cag Gln	atg Met	ggc Gly	ata Ile	1700
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cca Pro	gac Asp	agg Arg 420	agc Ser	aaa Lys	ctc Leu	cga Arg	gtg Val 425	tat Tyr	ctc Leu	cac His	tgc Cys	act Thr 430	aac Asn	gtc Val	tat Tyr	1892
cac His	cca Pro 435	cga Arg	tat Tyr	cag Gln	gaa Glu	gga Gly 440	gat Asp	cta Leu	act Thr	ctg Leu	tat Tyr 445	gtc Val	ctg Leu	aac Asn	ctc Leu	1940
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tcc Ser	aaa Lys	tct Ser	gtc Val 485	caa Gln	ctg Leu	aac Asn	Gly	caa Gln 490	att Ile	ctg Leu	aag Lys	atg Met	gtg Val 495	gat Asp	gag Glu	2084
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cta Leu	agc Ser 515	ctg Leu	cct Pro	gcc Ala	ttt Phe	tcc Ser 520	tat Tyr	ggt Gly	ttt Phe	ttt Phe	gtc Val 525	ata Ile	aga Arg	aat Asn	gcc Ala	2180
aaa	atc	gct	gct	tgt	ata	tgaa	aata	aa a	ggca	tacg	g ta	cccc	tgag	ſ		2228

Lys Ile Ala Ala Cys Ile 530 535 acaaaagccg aggggggtgt tattcataaa acaaaaccct agtttaggag gccacctcct tgccgagttc cagagettcg ggagggtggg gtacacttca gtattacatt cagtgtggtg ttctctctaa gaagaatact gcaggtggtg acagttaata gcactgtg 2396 <210> 46 <211> 385 <212> DNA <213> Rattus norvegicus <400> 46 eggeogetge tgetgetgtg getetggggg eggeteegtg eeetgaeeea aggeaeteeg gcggggaccg cgccgaccaa agacgtggtg gacttggagt tttacaccaa gaggctattc caaagcgtga gtccctcgtt cctgtccatc accatcgacg ccagtctggc caccgaccct 180 cggttcctca ccttcctgag ctctccacgg cttcgagccc tgtctagagg cttatctcct 240 gogtacttga gatttggcgg caccaagact gacttcctta tttttgatcc caacaacgaa 300 cccacctctg aagaaagaag ttactggcaa tctcaagaca acaatgatat ttgcgggtct 360 gaccgggtct ccgctgacgt gttga 385 <210> 47 <211> 541 <212> DNA <213> Rattus norvegicus <220> <221> misc_feature <222> (507)..(507) <223> Any nucleotide <400> 47 aaatcaggac atatcottca ottatttgcc tottggtcat attggaggca tttgtattca 60 tttttaataa ccctcaaaat agtgcatgca aagtgctaag cgtcatttgc cacatggtgc 120 cattaactgt caccacctgc agtggtctac ttagagaaca ccgcactgga tgttaacact 180 gaagcgcgtg coccgccctc ccgaggetet ggatccagcg ttgaagcttg ccccgccctc 240 ecgaggetet ggatecagea etggageatg eccegecete ecgaggetet ggagettget aaggagteeg etecetaeeg etggggtttt getttattet tatgaatgae acceetgaee 360 getttegtet eaggggtact gtaatgeett ttatttteat atacaagetg egattttgge 420

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480

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Leu Leu Leu Eu Trp Leu Trp Gly Arg Leu Arg Ala Leu Thr Gln Gly

Thr Pro Ala Gly Thr Ala Pro Thr Lys Asp Val Val Asp Leu Glu Phe $20 \hspace{1cm} 25 \hspace{1cm} 30$

Tyr Thr Lys Arg Leu Phe Gln Ser Val Ser Pro Ser Phe Leu Ser Ile 35 40 45

Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu Thr Phe Leu 50 60

Ser Ser Pro Arg Leu Arg Ala Leu Ser Arg Gly Leu Ser Pro Ala Tyr 65 70 75 80

Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Asn $85 \\ 90 \\ 95$

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Asn Asp Ile Cys Gly Ser Asp Asp Val Ser Ala Asp Val Leu 115 120 125

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Leu Lys Met Val Asp Glu Gln Thr Xaa Pro Ala Leu Thr Glu Lys Pro 1 $$ 10 $$ 15

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Phe Val Ile Arg Asn Ala Lys Ile Ala Ala Cys Ile 35 40